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PRINCIPAL INVESTIGATOR: Robert H. Hopper, Jr., Ph.D.

CONTRACTING ORGANIZATION: Inova Health Care Services
Alexandria, VA 22306-3209

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Robert H. Hopper, Jr., Ph.D.

E-Mail: rhopper@aori.org

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
This study will assess outcome after hip and knee joint replacement, testing the hypothesis that young patients are at increased risk for wear-related complications. We also hypothesize that periprosthetic bone loss, one of the most significant complications associated with implant wear, can be detected sooner and better monitored with routine follow-up that includes computed tomography imaging. Understanding the factors that influence the outcome of joint replacement procedures in the context of patient demands can help optimize surgical technique, implant selection, and post-operative management to insure the highest function and quality of life. Measuring implant wear and three-dimensional periprosthetic bone remodeling can help surgeons intervene at the appropriate time to prevent catastrophic implant failure. Institutional Review Board (IRB) approval for this study has been granted at the local level by Inova. We are currently working to obtain second level IRB approval from the United States Army Medical Research and Materiel Command (USAMRMC) Human Subjects Research Review Board (HSRRB). Although research work will not be initiated until IRB approval has been granted, we anticipate receiving second level approval in October 2007. As originally proposed, we expect that it will require 30 months to complete this research project once IRB approval has been obtained. Because we will not initiate research work until IRB approval has been granted, we anticipate filing for a no-cost extension corresponding to the period of time required to obtain IRB approval.

15. SUBJECT TERMS
Arthroplasty, Young, Hip, Knee, Wear, Osteolysis, Clinical Outcome, Three-Dimensional Imaging

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INTRODUCTION

Owing to the physically demanding nature of their professional responsibilities, active-duty military personnel are at risk for repetitive loading and traumatic injury that can lead to degenerative osteoarthritis. When conservative measures fail, joint replacement offers a reliable means to eliminate pain and restore function. While much research has been devoted to the surgical and post-operative management of elderly patients, less in known about the treatment and outcome of younger patient populations. This study will assess outcome after hip and knee joint replacement, testing the hypothesis that young patients are at increased risk for wear-related complications. We also hypothesize that periprosthetic bone loss, one of the most significant complications associated with implant wear, can be detected sooner and better monitored with routine follow-up that includes computed tomography imaging. For this study, a comprehensive institutional database will be used to retrospectively assess the survivorship and complications associated with hip and knee joint replacement among very young (at least 18 to less than 30 years old), young (age 30 to 50) and older patients (over 50 years of age at surgery). To improve post-operative monitoring protocols, three-dimensional imaging techniques for evaluating periprosthetic bone remodeling will be developed and validated. Understanding the factors that influence the outcome of joint replacement procedures in the context of patient demands can help optimize surgical technique, implant selection, and post-operative management to insure the highest function and quality of life. Measuring implant wear and three-dimensional periprosthetic bone remodeling can help surgeons intervene at the appropriate time to prevent catastrophic implant failure.

BODY

This research study will use outcome data accumulated in the Anderson Orthopaedic Research Institute's (AORI) clinical database over the past 25 years to develop a comprehensive understanding of implant wear and its consequences, particularly among young and high-demand patients. By quantifying the contributions of implant, patient, and surgical factors, implant selection can be optimized based on patient characteristics with the goal of reducing wear rates to mitigate long-term complications including wear through, implant loosening, and bone loss. Localized periprosthetic bone resorption, clinically known as osteolysis, can compromise implant fixation and is among the most significant long-term problems associated with joint arthroplasty. Although conventional x-rays provide a reliable means to measure implant wear, it is impossible to appreciate the three-dimensional volume of osteolysis using plain x-rays. While conventional computed tomography (CT) images can produce highly detailed images of anatomy, the x-rays used to produce CT images sometimes fail to penetrate the dense metal components used for joint replacements. When the CT image is reconstructed, the missing data generates streaks and other image artifacts that make it difficult to visualize and accurately analyze the periprosthetic anatomy. This study will develop imaging modalities enabling three-dimensional visualization and evaluation of periprosthetic anatomy to allow early detection and accurate measurement of osteolysis. Early detection and accurate monitoring of osteolytic lesion growth will

enable pharmaceutical or minimally invasive surgical intervention to treat progressive osteolysis that threatens implant stability.

We hypothesize that active-duty military personnel who require hip and knee joint replacements comprise a unique patient population with special requirements to insure that the procedure is successful. To avoid late complications, regular follow-up should be complimented with three-dimensional imaging of the periprosthetic anatomy. The cumulative effect of optimizing surgical technique, implant selection and post-operative management will enable improved outcome among young joint replacement patients.

The approved statement of work includes two main objectives that encompass several specific tasks as detailed below.

A. To retrospectively assess hip and knee joint replacement outcome stratified by patient age at surgery (Months 1-30):

1. Maintain and update a clinical database related to hip and knee joint replacement outcome (Months 1-30).
2. Measure hip and knee implant wear using clinical x-rays (Months 1-30).
3. Use multiple linear regression analyses to correlate implant, surgical and patient-related factors with prosthetic wear and clinical outcome (Months 21-30).
4. Evaluate survivorship and complications among very young (at least 18 to less than 30 years old), young (age 30 to 50 years old) and older patients (over 50 years of age at surgery) (Months 21-30).
5. Identify complications unique to young and very young joint replacement patient populations (Months 27-30).

B. To improve post-operative monitoring protocols (Months 1-30):

1. Optimize computed tomography image acquisition and explore other three-dimensional imaging modalities to minimize implant-induced artifacts (Months 1-12).
2. Develop methods to visualize three-dimensional periprosthetic anatomy (Months 1-12).
3. Devise analytical techniques to quantify three-dimensional periprosthetic bone remodeling (Months 1-12).
4. Evaluate osteolytic areas and bone defects on conventional x-rays (Months 1-24)
5. Validate three-dimensional image analysis techniques using sections from post-mortem retrieved specimens (Months 12-18).
6. Analyze digital CT images archived in AORI's database (Months 18-30).
7. Examine the correlation between osteolytic area based on conventional x-rays and volume measurements derived from CT images (Months 24-30).

8. Use multiple linear regression analyses to correlate implant, surgical and patient-related factors with the development of periprosthetic osteolysis (Months 24-30).
9. Develop follow-up protocols for CT imaging after total joint replacement (Months 27-30).

We are currently working to obtain Institutional Review Board (IRB) approval for this research study. Prior to submission of a study for IRB approval, the Inova Health System requires a formal Feasibility Study. Feasibility Study approval for this research was granted on December 6, 2006. Prior to submitting the IRB application to the Inova Health system for first-level local approval, the complete IRB application was submitted on March 13, 2007 for pre-review by the United States Army Medical Research and Materiel Command (USAMRMC) Human Subjects Research Review Board (HSRRB). We received comments from the USAMRMC HSRRB on March 26, 2007. We subsequently revised the IRB application to address these questions and concerns. The IRB application was submitted to the Inova IRB on May 30, 2007 and presented by Robert Hopper to the full Inova IRB at their meeting on June 20, 2007. Formal IRB approval from Inova was granted on June 20, 2007 and the IRB application was forwarded to the USAMRMC HSRRB on June 21, 2007. As of August 30, 2007, we were waiting on a response from the second level IRB review conducted by the USAMRMC HSRRB.

As originally proposed, we anticipate that it will require 30 months to complete this study once IRB approval has been granted. Because we will not initiate research work until IRB approval has been obtained, we anticipate filing for a no-cost extension corresponding to the period of time required to obtain IRB approval.

Although research work has not been initiated, we continue to develop the infrastructure and technology (Tasks B1, B2 and B3 as previously noted) to facilitate our future work. During the past year, Robert Hopper has dialogued with medical physicists, radiologists, radiology technicians, and manufacturer representatives regarding the optimal hardware and software configurations to facilitate this research study. We are also pursuing other collaborative relationships to facilitate our future work. Although this groundwork will enable us to use the most current technology when we initiate our research, the efforts devoted to this work have not been allocated to this study since we do not have IRB approval.

KEY RESEARCH ACCOMPLISHMENTS

Since research work will not be initiated until IRB approval is obtained, we have not yet made any scientific progress related to this project.

REPORTABLE OUTCOMES

Quarterly reports have been filed as specified in the Award Contract.

CONCLUSIONS

We are currently in the final phases of obtaining Institutional Review Board (IRB) approval for this study. Research work will not be initiated until IRB approval has been granted by our local IRB and the United States Army Medical Research and Materiel Command (USAMRMC) Human Subjects Research Review Board (HSRRB). As originally proposed, we anticipate that it will require 30 months to complete this research project once IRB approval has been granted. Because we will not initiate research work until IRB approval has been obtained, we anticipate filing for a no-cost extension corresponding to the period of time required to obtain IRB approval.

REFERENCES

None

APPENDICES

None